Seizure 22 (2013) 617–621

Contents lists available at SciVerse ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Clinical spectrum and treatment outcome of West Syndrome in children from Northern India

Jaya Shankar Kaushik, Bijoy Patra, Suvasini Sharma *, Dinesh Yadav, Satinder Aneja

Department of Pediatrics, Lady Hardinge Medical College and Associated Kalawati Saran Children's Hospital, New Delhi, India

ARTICLE INFO

Article history:
Received 18 December 2012
Received in revised form 12 April 2013
Accepted 14 April 2013

Keywords:
Epileptic encephalopathy
Hypsarrhythmia
Infantile spasms
Perinatal asphyxia
Symptomatic

ABSTRACT

Purpose: This study was intended to document the clinical profile and treatment outcome of West syndrome in children attending a tertiary care center in Northern India.
Method: Data were collected by a retrospective chart review of children diagnosed with West syndrome between January 2008 and January 2012. Information was recorded pertaining to the age at onset and presentation, etiology, and associated co-morbidities; results of electroencephalography (EEG) and neuroimaging; treatment given; and final outcome. The following drugs were used for treatment: pyridoxine, prednisolone, vigabatrin, sodium valproate, nitrazepam, topiramate, and levetiracetam. The response was categorized as spasm cessation, partial improvement (>50% improvement), or no improvement. The final outcome was considered favorable when there was a complete cessation of spasms; with absence of relapse and no progression to other seizure types for at least 6 months.
Results: Records of 148 children (120 boys) were analyzed. The mean (SD) age at onset and presentation was 5.3 (4.6) months, and 13.1 (7.3) months, respectively. Perinatal asphyxia (61.4%), neonatal sepsis/meningitis (10.6%), and postnatal meningitis (11.4%) were the predominant causes. The etiology could not be ascertained in 16.6% of children. Favorable outcome was observed in 45 (30.4%) children with spasm cessation rate of 25.4% with prednisolone. Age at onset, gender, time lag to treatment, presence of perinatal asphyxia, or co-morbid cerebral palsy did not affect the final outcome.
Conclusion: This study highlights the developing country perspective of children with West syndrome, including delayed presentation, adverse perinatal events as the predominant etiology, and modest response to oral steroids.

1. Introduction

West syndrome is an epileptic encephalopathy characterized by epileptic spasms, electroencephalographic evidence of hypsarrhythmia, and developmental delay or regression. The peak age of onset is 4–7 months.[1] The etiology is highly heterogeneous and includes cortical malformations, neurocutaneous syndromes, inherited metabolic disorders, perinatal brain injuries (asphyxia, hypoglycemia, sepsis, and meningitis), and postnatal acquired brain injuries such as meningitis and head trauma. Based on etiology, West syndrome is classified as symptomatic with known etiology and cryptogenic or (unknown etiology).[2] The symptomatic group represents 60–80% of cases. West syndrome is a difficult-to-treat disorder characterized by poor response to antiepileptic drugs and consequent intellectual disability.

Information on the profile of infants with West syndrome in developing countries is limited.[3–6] Management of children in resource-constrained settings is limited by delay in presentation and high cost of drugs such as adrenocorticotrophic hormone (ACTH) and vigabatrin. Hence, this retrospective study was conducted to evaluate the clinical profile and treatment outcome of children with West syndrome in a developing country scenario.

2. Methodology

This study was conducted at the pediatric department of Lady Hardinge Medical College and Kalawati Saran Children Hospital, a tertiary care government-sponsored teaching hospital in New Delhi, India. The patients seeking treatment in this hospital belong to Delhi and surrounding rural districts of Haryana, Uttar Pradesh, and Punjab. These patients predominantly belong to the lower socioeconomic status and do not have any form of health insurance.

2.1. Patient selection

Data were collected by a retrospective chart review of all patients diagnosed with West syndrome between January 2008

* Corresponding author. Tel.: +91 9910234344.
E-mail address: sharma.suvasini@gmail.com (S. Sharma).

1059-1311/$ – see front matter © 2013 British Epilepsy Association. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.seizure.2013.04.014

and January 2012. Medical records of patients who were followed for less than 6 months were excluded. The diagnosis of West syndrome was based on the presence of epileptic spasms, along with electroencephalographic (EEG) findings of hypsarrhythmia or its variants. Hypsarrhythmia was defined as EEG showing high-voltage chaotic slow waves intermixed with spike and sharp wave discharges. Modified hysparrythmia was defined in presence of any of the following: increased interhemispheric synchronization-consistent voltage asymmetries; consistent focus of abnormal discharge; episodes of generalized/regional or lateralized voltage attenuation; or primarily high-voltage bilaterally asynchronous slow wave activity.[7]

2.2. Baseline clinical data

The following data were collected from the case records: sex, age of onset of infantile spasms, age at diagnosis, and the type of spasms. The average number of spasms per cluster and number of clusters per day was recorded. The frequency of spasms was noted from parent-maintained seizure dairy or parental recall during visits. History of sleep problems, feeding problems, and presence of repeated chest infections was also noted. The 'lag time' was defined as the time from initial observation of spasms to diagnosis.

History of perinatal events, developmental milestones and relevant family events was recorded. The diagnosis of birth asphyxia was considered when the delayed cry at birth was followed with features of neonatal encephalopathy. Physical examination findings suggestive of cerebral palsy, microcephaly, presence of neurocutaneous markers, dysmorphism, and organomegaly were documented.

2.3. Investigations

The results of EEG and neuroimaging (CT/MRI) were noted. Computed tomography (CT) scan was the initial investigation in children where there was a clear history suggestive of perinatal insult, postnatal meningitis, or encephalitis. Magnetic resonance imaging (MRI) was performed in all the other cases, and in cases where the CT scan was normal. Children with clinical suspicion of metabolic disorders (a history of parental consanguinity, prior affected siblings, unexplained vomiting, intermittent worsening of symptoms, recurrent episodes of lethargy, altered sensorium, or ataxia or hepatosplenomegaly on examination) or no obvious etiology on clinical evaluation and neuroimaging were screened for inherited metabolic disorders based on reports of arterial blood gas, blood lactate, blood ammonia, urine ketones, and blood tandem mass spectrometry. Based on the etiology, West syndrome was classified as symptomatic (known etiology) or cryptogenic (unknown etiology).

2.4. Treatment protocol

Available treatment options included prednisolone, pyridoxine, sodium valproate, vigabatrin, nitrazepam, topiramate, and levetiracetam. Treatment options varied according to the affordability of the treatment for the patient and associated infection and malnutrition. Prednisolone and sodium valproate are available free from the hospital. The usual protocol at our center is to start with a trial of pyridoxine (15 mg/kg/day) for 3–7 days (Fig. 1). In pyridoxine unresponsive patients, oral prednisolone (2 mg/kg/day) was given. Patients who were severely malnourished or had evidence of active tuberculosis were not administered steroids. These patients were treated with vigabatrin. Those who failed steroids were also started on vigabatrin if the parents could afford it. Otherwise, the treatment options included sequential trials of sodium valproate, nitrazepam, topiramate, and levetiracetam

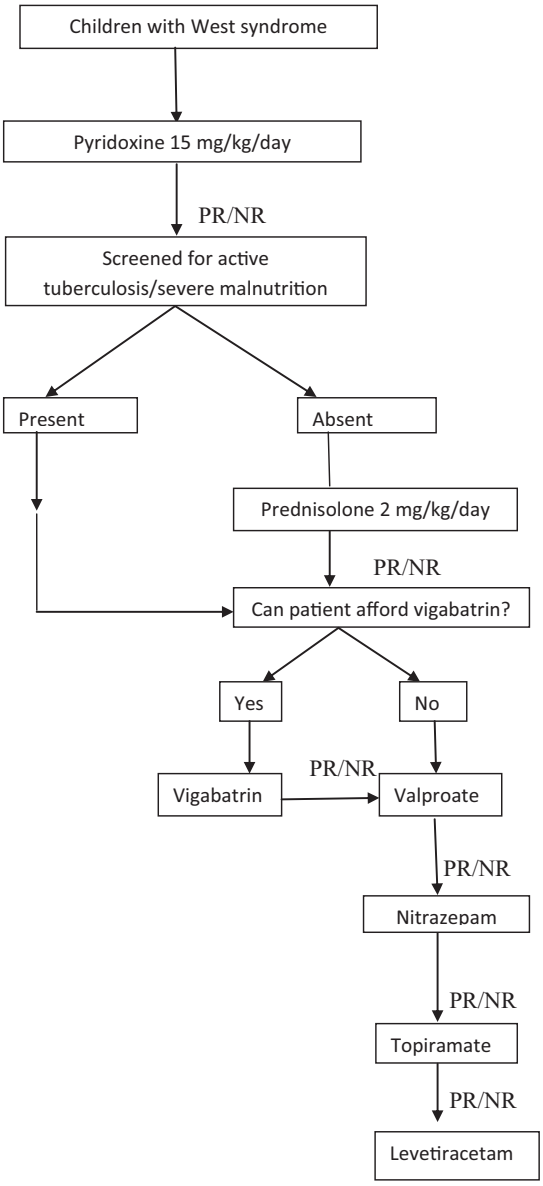

Fig. 1. Flow chart of treatment protocol of West syndrome at our center (NR, no response; PR, partial response).

(Fig. 1). The treatment received by the patient and the response in terms of spasm reduction or cessation was noted. The treatment protocol was modified if the drugs in next sequence had already been tried. Treatment response was classified as spasm cessation when there was a complete cessation of spasms, *partial response* when >50% improvement was observed, and *poor response* when there was <50% improvement; two weeks after starting the drug.

2.5. Follow-up records

Records of follow-up were studied to determine the response to treatment, any evidence of relapse, and progression to other seizure types. EEG was repeated in patients who developed a relapse or progressed to have other seizure types and in those with spasm cessation to document resolution of hypsarrhythmia. An EEG was also repeated if the patient developed a relapse or progressed to have other seizure types. The final outcome was considered *favorable* when there was a complete spasm cessation for at least 6 months without relapse or progression to other

seizure types. The presence of favorable outcome was studied in relation to the etiology and clinical variables at presentation.

2.6. Analysis

The data were entered by two investigators (JSK and SS) into separate Microsoft Excel sheets, the sheets were compared, and any inconsistency was cross-checked with the original data. Categorical variables were presented as proportions; their association with the final outcome was compared using the chi-square test. Continuous variables were presented as mean (SD) and their associations with the final outcome were compared using the unpaired Student's *t*-test. The level of significance was assumed at 5%. Multivariate logistic regression was applied keeping the final outcome (favorable outcome) as the dependent variable. Independent variables considered in model included; age at onset (in months), time lag to treatment (in months), gender, history of neonatal intensive care unit (NICU) stay (yes/no), and etiology. The statistical analysis was done using SPSS 17.0 version.

3. Results

3.1. Clinical and demographic profile

Records of 148 children were finally analyzed (records identified: 156; excluded for inadequate follow up: 8) (Table 1). The age at onset of spasms ranged from 1 month to 30 months [mean 5.3 (4.6) months]. The mean (SD) age at diagnosis of West syndrome was 13.1 (7.2) months. The mean (SD) lag time to treatment was 7.9 (7.4) months. There was a male preponderance [n = 120 (81.1%)] in our study. The median duration of follow-up was 12 months (range 6–43 months). Developmental delay prior to the onset of spasms was present in 137 (92.5%) patients. EEG findings were compatible with hypsarrhythmia in 63 (42.4%) children; and with modified hypsarrythmia in the rest (57.6%).

Table 1
Baseline clinical profile of children with West syndrome (N = 148).

Baseline characteristics	Values
Mean (SD)	
Age at spasm onset in months	5.3 (4.6)
Age at diagnosis in months	13.1 (7.3)
Lead time in months	7.9 (7.4)
Number of clusters per day	12.4 (8.8)
Number of spasms per cluster	4.8 (2.1)
Number (%)	
Male gender	120 (81.1%)
Type of spasm	
Flexor	113 (76.3%)
Extensor	9 (6.2%)
Mixed	26 (17.6%)
Development prior to spasm onset	
Delayed	137 (92.5%)
Normal	11 (7.4%)
Microcephaly	96 (64.9%)
Cerebral palsy	92 (62.2%)
Spastic quadriplegic	82 (55.4%)
Spastic diplegic	8 (5.4%)
Spastic hemiplegic	2 (1.4%)
Comorbidities	
Visual impairment	35 (23.6%)
Hearing impairment	15 (10.1%)
Sleep disturbances	9 (6.1%)
Feeding difficulties	15 (10.1%)
Recurrent chest infections	7 (4.7%)

Table 2
Etiology of West syndrome in the study population.

Etiology	Number (%) (N = 148)
Symptomatic (known etiology)	122 (82.4%)
Prenatal causes	
Cortical migration defects	5 (4.1%)
Intrauterine infections	2 (1.6%)
Inherited metabolic disorders	2 (1.6%)
Tuberous sclerosis	1 (0.8%)
Perinatal causes	
Birth asphyxia	75 (61.4%)
Neonatal sepsis/meningitis	13 (10.6%)
Neonatal hypoglycemia	5 (4.1%)
Prematurity	3 (2.4%)
Perinatal stroke	1 (0.8%)
Postnatal causes	
Meningitis/meningoencephalitis	14 (11.4%)
Unknown etiology	26 (17.5%)

Almost two-thirds of the children had flexor spasms with the rest having mixed or extensor spasms. The enrolled children had an average 10 clusters per day, with each cluster having 5 spasms. Relationship of spasms with the sleep–wake cycle was observed in 108 (72.9%) children. There were 13 (8.4%) children who were small for gestational age.

3.2. Etiology

In our study, the majority of the children were symptomatic [122 (82.4%)]; etiology could not be ascertained in the rest. Perinatal brain injury was the leading cause of West syndrome, seen in 81 children (66.3%) (Table 2). Among the perinatal causes, birth asphyxia was the predominant. Neonatal sepsis/meningitis (13), neonatal hypoglycemia (5), prematurity (3), kernicterus (1), and perinatal stroke (1) were the other perinatal etiologies. Postnatal causes included meningitis and meningoencephalitis in 14 children. Prenatal causes included malformations of cortical development (5), intrauterine infections (2), tuberous sclerosis (1), and inherited metabolic disorders (2).

3.3. Treatment response

Drugs used in our study for treatment of children with West syndrome included pyridoxine (135), prednisolone (122), sodium valproate (110), vigabatrin (47), nitrazepam (27), topiramate (16), and levetiracetam (9). The response to treatment is depicted in Table 3. Complete spasm cessation occurred in only one patient with pyridoxine. With the use of oral prednisolone, complete spasm cessation was observed in 31 (25.4%), while an additional 31.9% showed a partial response. Eighteen (16%) children achieved complete spasm cessation with sodium valproate, and 13 (27.6%) with vigabatrin. A repeat EEG could be obtained in 65 children with complete spasm cessation; 19 were normal and hypsarrhythmia persisted in 12 children. Hypsarrhythmia resolved with presence of background and other epilepitiform abnormalities in 34 children.

3.4. Factors predicting favorable outcome

Forty-five children had a favorable outcome. The age at onset, gender, or lag time for treatment initiation was not found to have any significant role in predicting a favorable outcome (Table 4).

Table 3
Response to treatment among children of West syndrome ($N = 148$).

Drugs	Number tried	Spasm cessation	Partial response (>50% improvement)	No response (<50% improvement)
Pyridoxine	135 (91.2%)	1 (0.7%)	12 (8.9%)	122 (90%)
Prednisolone	122 (82.4%)	31 (25.4%)	39 (32%)	52(42.6%)
Sodium valproate	110 (74.3%)	18 (16.3%)	37 (33.6%)	55 (50%)
Vigabatrin	47 (31.7%)	13 (27.6%)	10 (21.3%)	24 (51.1%)
Nitrazepam	27 (18.2%)	5 (18.5%)	8 (29.6%)	14 (51.8%)
Topiramate	16 (10.8%)	3 (18.8%)	6 (37.5%)	7 (43.7%)
Levetiracetam	9 (6.1%)	0	5 (55.5%)	4(44.4%)

Symptomatic cases had an unfavorable outcome as compared to children in whom no underlying etiology could be found ($P = 0.05$). Multivariate logistic regression revealed that male gender [OR 1.377 (95% CI 0.562–3.372) ($P = 0.484$)], history of NICU stay [OR 1.06 (95% CI 0.495–2.295) ($P = 0.871$)], symptomatic etiology [OR 1.866 (95% CI 0.728–4.888) ($P = 0.192$)], age at onset [OR 0.994 (95% CI 0.917–1.076) ($P = 0.873$)] and time lag to treatment [OR 1.033 (95% CI 0.976–1.093) ($P = 0.265$)] did not affect the final outcome.

4. Discussion

This was a large retrospective study of children with West syndrome conducted in resource-constrained settings of a developing country. We observed that symptomatic West syndrome formed a major group (82%) and that was significantly associated with an unfavorable outcome. Age at onset, etiology, and lag time in treatment did not effect the final outcome. Our study highlights the clinical spectrum, treatment response, and predictors of outcome in children with West syndrome, hence providing a developing country perspective. The challenges faced in our setting include delayed presentation; inability for patients to procure expensive medications like ACTH, vigabatrin, and levetiracetam; and difficulty in admitting the patient to the inpatient setting for ACTH treatment owing to overcrowding in the hospital and the risk of developing cross infections.

The mean age at onset of infantile spasms (5.3 months) was comparable to experience at other centers.[8–10] Mean lag time in treatment initiation in most of the Western studies varies between 25 and 45 days.[8–10] The lag time was significantly higher in our study, likely owing to the health-seeking behavior of parents; lack of awareness on this ailment among the pediatricians; and use of inappropriate antiepileptics such as phenobarbitone, phenytoin, and carbamazepine. These are acknowledged as lacunae in the treatment of children in the developing countries.[3,4] Surprisingly, we did not find any association of the lag time with the final outcome. This is in contrast to earlier studies, that demonstrated better long term outcome in children with early treatment initiation.[6,11] Improving awareness of clinicians and parents about infantile spasms and helping them differentiate it from abdominal colic or startle reflex might reduce the lag time. We acknowledge that the relatively small sample size of our study could also probably influence the impact of lag time to treatment on the final outcome.

We found a striking male preponderance in our study, probably owing to gender-biased referral and treatment-seeking behavior of parents. This gender bias is well rooted in the traditional culture of the Indian society where male children are brought to medical attention more frequently and females are neglected. These findings are similar to other studies from the Indian subcontinent.[3,4] We observed that 92.5% of children had developmental delay preceding the onset of spasms. In our study, almost two-thirds of children were microcephalic and half had comorbid spastic quadriplegic cerebral palsy. These findings are consistent with previous reports.[3,4,12] However, we did not observe the effect of these parameters on the final outcome. High rates of comorbidities such as cerebral palsy, microcephaly, vision and hearing impairment, and feeding difficulties as sequelae of perinatal insults are additional problems in children with West syndrome in our scenario.

The proportion of symptomatic cases is higher in our scenario as compared to Western data. In the United Kingdom infantile spasms study, a known etiology could be demonstrated in 61% of the cases, whereas in our study, 82% of the patients had a known etiology.[13] The etiological profile in our study was also considerably different from the West. The most common cause of was a perinatal brain injury, especially perinatal asphyxia. In contrast, prenatal causes which include cortical malformations, neurocutaneous syndromes, and genetic–metabolic disorders are the predominant etiologies in the West.[13–15] High incidence of perinatal asphyxia in our study setting could be attributed to lack of antenatal care, high rates of home delivery, delivery by unskilled workers, delay in treatment initiation, and a poor referral system. Improvement in the maternal and neonatal health services may help in reducing the incidence of West syndrome in developing countries.

We found a spasm cessation rate of 25.4% with oral prednisolone. In the doses used (2 mg/kg/day), oral prednisolone has been shown to be less effective as compared to ACTH. Spasm freedom rates ranging from 25% to 33% have been found at this dose, compared to 70% response rate with ACTH.[16–18] Our response rates

Table 4
Factors affecting the final outcome.

Factors	Favorable outcome ($N = 45$)	Unfavorable outcome ($N = 103$)	P value
Mean (SD)			
Age at onset (months)	5.6 (5.3)	5.2 (4.2)	0.65
Time lag (months)	6.9 (5.7)	8.3 (7.9)	0.29
Proportions			
Male gender	35 (77.8%)	85 (82.5%)	0.50
Birth asphyxia	22 (48.9%)	55 (53.4%)	0.61
NICU stay	20 (44.4%)	53 (51.5%)	0.43
Neonatal sepsis	9 (20%)	23 (22.3%)	0.75
Spastic quadriplegia	24 (53.3%)	58 (56.3%)	0.89
Microcephaly	27 (60%)	69 (67%)	0.41
Symptomatic etiology	34 (75.6%)	88 (85.4%)	0.05

are comparable to past literature, though we have the additional problem of delayed presentation which may have also reduced the responder rates. Recent data suggest that the use of high-dose prednisolone (40–60 mg/day) may be as effective as ACTH.[19,20] In the United Kingdom infantile spasms study, spasm freedom was achieved in 70% of children taking high-dose oral prednisolone (40 mg/day) and 76% of children taking ACTH (40 IU/alternate day).[19] The risks of using the high-dose steroid in developing countries like India, especially infections, have to be balanced with the advantages. A randomized trial comparing the usual dose (2 mg/kg/day) and high dose (4 mg/kg/day) in children with newly diagnosed West syndrome is now in progress at our center (Clinical Trials.Gov identifier NCT01575639).

As vigabatrin is expensive, it was offered only to those patients who failed steroids and were able to afford it. In our study, out of 47 such patients, 13 had spasm freedom accounting to the responder rate of 27.6%. This is lower than the 54% response rate reported in the literature,[19] but this is likely due to the delay in treatment initiation and use as a second-line agent. Other drugs such as sodium valproate, topiramate, and nitrazepam showed modest efficacy ranging from 16% to 19%, which is lower than previous reported literature,[21–23] but could be accounted for by the fact that these drugs were used as second- and third-line agents, which might have resulted in reduced efficacy. Pyridoxine was also not found to be a useful agent, contrary to reports from Japan, where this agent has been used extensively for the treatment of infantile spasms.[24] Only one child in our cohort was pyridoxine responsive. Hence, we consider that the pyridoxine drug trial may not be warranted in our setting. Perhaps the response may improve with higher doses or the use of other formulations such as pyridoxal phosphate.[25]

In our study, we preferred the term "favorable outcome" instead of treatment success and treatment failure, considering that EEG evidence of hypsarrhythmia might persist despite cessation of clinical spasms. Definition of favorable outcome was more clinically relevant and parent-centered.

The limitations of the study include the absence of long-term video-EEG monitoring for assessing treatment outcomes and lack of long-term follow-up. Lack of long-term follow-up is difficult in our study setting owing to the large proportion children who belong to the migrant population in Delhi. Also, we did not objectively assess the developmental outcome. Another limitation to be considered while assessing treatment outcomes is that the natural history of spasms must be taken into account, with the possibility of spontaneous remission. This is all the more important in our scenario with delayed presentation. However, despite these shortcomings, the data of this large number of patients gives us an insight into the challenges faced in the management of West syndrome in resource constrained settings.

In conclusion, we describe the clinico-etiological profile and treatment outcome of children with West syndrome in a developing country scenario. The commonest etiology was perinatal brain injury, especially birth asphyxia. There was a prolonged lag time between the onset of spasms and initiation of treatment. Symptomatic etiology was associated with an unfavorable outcome.

Competing interests

None.

Funding source

None.

Acknowledgments

We wish to thank Mr Rajeev Kumar (MPhil), Biostatistician, Department of Biostatistics, University College of Medical Sciences, New Delhi, for help with the statistical analysis; and Dr Prakash Poudel, Associate Professor, Department of Pediatrics, B.P. Koirala Institute of Health Sciences, Dharan, Nepal, for assistance with data collection. Dr Poudel was an observer in our department at the time of the conduct of the study.

References

1. Sakakihara Y. Treatment of West syndrome. *Brain and Development* 2011;**33**:202–6.
2. Watanabe K. West syndrome: etiological and prognostic aspects. *Brain and Development* 1998;**20**:1–8.
3. Singhi P, Ray M. Profile of West syndrome in North Indian children. *Brain and Development* 2005;**27**:135–40.
4. Kalra V, Gulati S, Pandey RM, Menon S. West syndrome and other infantile epileptic encephalopathies – Indian hospital experience. *Brain and Development* 2001;**23**:593–602.
5. Malik MA, Tarrar MA, Qureshi AO, Zia-Ur-Rehman M. Clinical spectrum of infantile spasm at presentation. *Journal of College of Physicians and Surgeons Pakistan* 2012;**22**:31–4.
6. Sharma NL, Vishwanthan V. Outcome in West syndrome. *Indian Pediatrics* 2008;**45**:559–63.
7. Hrachovy RA, Frost Jr JD, Kellaway P. Hypsarrhythmia: variations on the theme. *Epilepsia* 1984;**25**:317–25.
8. Cohen-Sadan S, Kramer U, Ben-Zeev B, Lahat E, Sahar E, Nevo Y, et al. Multicenter long-term follow-up of children with idiopathic West syndrome: ACTH versus vigabatrin. *European Journal of Neurology* 2009;**16**:482–7.
9. Lagae L, Verhelst H, Ceulemans B, De Meirleir L, Nassogne MC, De Borchegrave V, et al. Treatment and long term outcome in West syndrome: the clinical reality. A multicentre follow up study. *Seizure* 2010;**19**:159–64.
10. Zhu X, Chen O, Zhang D, Jin R, Li F, Wang Y, et al. A prospective study on the treatment of infantile spasms with first-line topiramate followed by low-dose ACTH. *Epilepsy Research* 2011;**93**:149–54.
11. O'Callaghan FJ, Lux AL, Darke K, Edwards SW, Hancock E, Johnson AL, et al. The effect of lead time to treatment and of age of onset on developmental outcome at 4 years in infantile spasms: evidence from the United Kingdom Infantile Spasms Study. *Epilepsia* 2011;**52**:1359–64.
12. Lee WL, Ong HT. Epidemiology of West syndrome in Singapore. *Brain and Development* 2001;**23**:584–5.
13. Osborne JP, Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, et al. The underlying etiology of infantile spasms (West syndrome): information from the United Kingdom Infantile Spasms Study (UKISS) on contemporary causes and their classification. *Epilepsia* 2010;**51**:2168–74.
14. Cowan LD, Hudson LS. The epidemiology and natural history of infantile spasms. *Journal of Child Neurology* 1991;**6**:355–64.
15. Trevathan E, Murphy CC, Yeargin-Allsopp M. The descriptive epidemiology of infantile spasms among Atlanta children. *Epilepsia* 1999;**40**:748–51.
16. Hrachovy RA, Frost Jr JD, Kellaway P, Zion T. A controlled study of prednisone therapy in infantile spasms. *Epilepsia* 1979;**20**:403–7.
17. Baram TZ, Mitchell WG, Tournay A, Snead OC, Hanson RA, Horton EJ. High-dose corticotropin (ACTH) versus prednisone for infantile spasms: a prospective, randomized, blinded study. *Pediatrics* 1996;**97**:375–9.
18. Hrachovy RA, Frost Jr JD, Kellaway P, Zion TE. Double-blind study of ACTH vs prednisone therapy in infantile spasms. *Journal of Pediatrics* 1983;**103**:641–5.
19. Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, Newton RW, et al. The United Kingdom Infantile Spasms Study comparing vigabatrin with prednisolone or tetracosactide at 14 days: a multicentre, randomised controlled trial. *Lancet* 2004;**364**:1773–8.
20. Kossoff EH, Hartman AL, Rubenstein JE, Vinning EP. High-dose oral prednisolone for infantile spasms: an effective and less expensive alternative to ACTH. *Epilepsy & Behavior* 2009;**14**:674–6.
21. Siemes H, Spohr HL, Michael T, Nau H. Therapy of infantile spasms with valproate: results of a prospective study. *Epilepsia* 1988;**29**:553–60.
22. Korinthenberg R, Schreiner A. Topiramate in children with west syndrome: a retrospective multicenter evaluation of 100 patients. *Journal of Child Neurology* 2007;**22**:302–6.
23. Chamberlain MC. Nitrazepam for refractory infantile spasms and the Lennox-Gastaut syndrome. *Journal of Child Neurology* 1996;**11**:31–4.
24. Tsuji T, Okumura A, Ozawa H, Ito M, Watanabe K. Current treatment of West syndrome in Japan. *Journal of Child Neurology* 2007;**22**:560–4.
25. Ohtahara S, Yamatogi Y, Ohtsuka Y. Vitamin B(6) treatment of intractable seizures. *Brain and Development* 2011;**33**:783–9.